

Application No. 10/731,741

Reply to final office action dated: September 11, 2006

Response dated: October 30, 2006

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (currently amended) An *in vitro* system comprising a cell preparation comprising OP9 stromal cells that have been modified to express a Notch ligand that supports T cell lymphopoiesis but does not support B cell lymphopoiesis of stem cells or progenitor cells, wherein the Notch ligand is Delta-like-1 or Delta-like-4 and wherein the T cells produced comprise T cells of one or more of the following lineages:

(a) ~~CD4<sup>-</sup>CD8<sup>-</sup>CD25<sup>+</sup>CD44<sup>+</sup> double negative (DN) T cells;~~

(b) ~~TCR- $\alpha\beta$ <sup>+</sup>CD4<sup>+</sup>CD8<sup>+</sup> double positive (DP) T cells;~~

(e)(a) TCR- $\alpha\beta$ <sup>+</sup> CD4<sup>-</sup>CD8<sup>+</sup> T cells; and/or

(d)(b) TCR- $\gamma\delta$ <sup>+</sup> T cells.

2. (previously presented) An *in vitro* system of claim 1 wherein the Notch ligand induces T cell lineage commitment and differentiation, stage-specific progenitor expansion, TCR gene rearrangement, and T cell differentiation by hematopoietic progenitors and embryonic stem cells in the absence of the thymus.

3. (cancelled).

4. (currently amended) An *in vitro* system of claim 1, wherein the stem cells or progenitor cells are selected from hematopoietic progenitor cells, hematopoietic stem cells and embryonic stem cells. that induces TCR V(D)J rearrangement, and T cell differentiation by hematopoietic progenitor cells or embryonic stem cells.

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5. – 9. (cancelled).

10. (previously presented) An *in vitro* system as claimed in claim 1 wherein the OP9 cells comprise a Delta-like-1 nucleic acid sequence shown in SEQ ID NO:8 or SEQ ID NO:9.

11. (previously presented) An *in vitro* system as claimed in claim 1 wherein the OP9 cells comprise a Delta-like-4 nucleic acid sequence shown in SEQ ID NO:10 or SEQ ID NO:11.

12. (previously presented) A method of forming cells of the T cell lineage comprising culturing stem cells or progenitor cells that are capable of differentiating into cells of the T cell lineage with an *in vitro* system of claim 1 to form cells of the T cell lineage.

13. (original) A method according to claim 12 wherein the cells that are capable of differentiating into cells of the T lineage are selected from hematopoietic progenitor cells, hematopoietic stem cells and embryonic stem cells.

14. – 16. (cancelled).

17. (currently amended) A method of claim ~~14~~12 wherein the ~~population of formed~~ cells are formulated in a pharmaceutically acceptable carrier, auxiliary or excipient.

18. – 21. (cancelled).

22. (currently amended) A method for expanding cells of the T cell lineage comprising:

- (a) culturing stem cells or progenitor cells capable of differentiating into cells of the T cell lineage with ~~a system of claim 1~~ an *in vitro* system comprising a cell

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preparation comprising OP9 stromal cells that have been modified to express a Notch ligand that supports T cell lymphopoiesis but does not support B cell lymphopoiesis of stem cells or progenitor cells, wherein the Notch ligand is Delta-like-1 or Delta-like-4 and wherein the T cells produced comprise T cells of one or more of the following lineages:

(i) CD4<sup>-</sup> CD8<sup>-</sup> CD25<sup>+</sup> CD44<sup>+</sup> double negative T cells;

(ii) CD4<sup>-</sup> CD8<sup>-</sup> CD25<sup>+</sup> CD44<sup>+</sup> double negative T cells;

(ii) TCR- $\alpha\beta$ <sup>+</sup> CD4<sup>+</sup> CD8<sup>+</sup> double positive T cells;

(iii) TCR- $\alpha\beta$ <sup>+</sup> CD4<sup>-</sup> CD8<sup>+</sup> T cells; and/or

(iv) TCR- $\gamma\delta$ <sup>+</sup> T cells; and

(b) isolating increased numbers of the T cell lineage, wherein the number of cells is increased by at least about 10 to 15 fold.

23. - 49. (cancelled).